The Assessment of Arterial Compliance Using Noninvasive Techniques: A Comparison of Radial and Occlusive Measures of Arterial Pressure and Flow

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Background: Nitric Oxide (NO) plays a pivotal role in controlling the tone of arteries. Modulation of NO, by using the donor Glycerol Timitrate (GTN) or the inhibitor N\(^2\)-Nitro-L-arginine methyl ester (L-NAME) alters arterial tone. Changes in vascular tone have traditionally been assessed in terms of steady-state haemodynamics. These ignore the importance of the pulsatile component of the circulation. This component can be derived from analysis of the arterial pressure pulse contour recorded non-invasively. In this study we have compared the use of radial tonometry with novel ocular measures of arterial pressure and flow. Methods: 10 healthy male volunteers had baseline radial artery pressure recorded using the OBF Pneumotonometer (CHT 2000). Doppler ultrasound measures of flow in the ocular arteries was made, using the ATLMADI 3500 device. Ocular pressure was recorded directly using the OBF Pneumotonometer. 0.5 milligrams GTN was administered sublingually. The above were then repeated after 3 minutes. A rest period of ten minutes ensued after the above procedure. The above were then repeated after 3 minutes. A rest period of ten minutes ensued after the above procedure. All measures were repeated after the dose increment and at the end. Results: No significant change in Cardiac Output (CO) occurred with GTN. Large arterial compliance was significantly improved by GTN, as was ocular compliance. The radial and ocular waveforms changed significantly and consistently. GTN was significantly decreased with L-NAME but this was confounded by the reduction in heart rate. Small arterial compliance was significantly reduced in a dose-dependent fashion. A marked alteration in the pulse waveforms was detected with L-NAME. These changes were similar at both the radial and ocular sites. Conclusions: Non-invasive measures of arterial tone can track changes in the vasculature in a sensitive manner. Pronounced changes occurred in both the derived pulsatile parameters and the waveforms in response to changes in NO. Occlusive measures of arterial flow are comparable to radial studies and provide a unique and novel method for assessing the microcirculation non-invasively.

Ocular Measures of Arterial Pressure and Flow: Noninvasive Techniques: A Comparison of Radial and Ocular Pressure in Healthy Volunteers

Background: Endothelial dysfunction is a known contributor to coronary disease. It is unclear what the additive contribution of traditional risk factors and genetic polymorphisms is on vascular reactivity in women with ischemic syndromes, and through what mechanisms.

Methods: We studied 79 WISE women who underwent coronary angiography for suspected ischemia. Average peak velocity ratio (APV-R) response to acetylcholine (Ach), which produces endothelium-dependent vasodilation, was measured. Linear regression was used to determine the joint effects of covariates on APV-R. Variables analyzed for inclusion in the model were: age, race, \( \beta \)-adrenergic receptor (AR), \( \beta \)-AR, and Gs gene variants, SBP, DBP, BMI, diabetes, hypertension, dyslipidemia, coronary artery disease, CAD severity score, smoking status, ever oral contraceptive (OC) use, ever HRT use, ACE inhibitor use, statin, and menopausal status.

Results: The model of best fit (R\(^2\) = 0.34, <0.001) included the non-genetic variables history of hypertension (p = 0.065), current smoker (p = 0.0004), SBP (p = 0.046), and ever OC use (p = 0.003). These variables were retained in the model. A reduction in arterial pressure pulse contour was noted, with a significant 10% to 20% reduction in systolic and diastolic arterial pressure levels. The CAD severity score was found to be significant in predicting APV-R response, with a 14% reduction in APV-R with each increase in CAD severity score. APV-R response was significantly less with diabetes than without diabetes (p = 0.02). These findings suggest that administration of irbesartan and/or lipoic acid to patients with the metabolic syndrome improves endothelial function and reduces pro-inflammatory markers, factors which are implicated in the pathogenesis of atherosclerosis.

Effects of irbesartan and Lipoic Acid on Endothelial Function and Serum Inflammatory Markers in Patients With the Metabolic Syndrome

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Background: The metabolic syndrome is associated with an increased incidence of early or accelerated atherosclerosis. An increased activity of angiotensin II induction of the vascular oxidative state, and endothelial dysfunction are significant factors in the pathogenesis of atherosclerosis. We wished to investigate the effects of irbesartan, an angiotensin receptor blocker, and lipoic acid, an antioxidant, on endothelial function in patients with the metabolic syndrome.

Methods: We enrolled 32 subjects that met the criteria for the metabolic syndrome into the study. The subjects were randomized to placebo (Group A, n = 8), 150mg/day irbesartan (Group B, n = 8), 1 g/day lipoic acid (Group C, n = 8), or irbesartan and lipoic acid (Group D, n = 8) for 4 weeks. Serum levels of interleukin-6 and inter leukin-6 (IL-6) were measured. Endothelial dependent flow mediated vasodilation (FMD) was also determined.

Results: The FMD was significantly increased in Group B (38.6 ± 7.3 to 66.6 ± 10.0% p < 0.005), Group C (42.5 ± 6.4 to 61.6 ± 8.0%, p < 0.005), and Group D (40.8 ± 8.1 to 72.2 ± 8.4%, p < 0.005). Serum levels of isoprostanes were reduced in Group B (44.3 ± 6.5 to 57.6 ± 7.4 pg/ml, p < 0.005) and Group C (47.6 ± 6.3 to 56.2 ± 5.7 pg/ml, p < 0.005); no significant changes were noted in Groups A or C. There was a reduction in serum IL-6 in Group B (11.1 ± 1.0 to 9.7 ± 1.2 pg/ml, p < 0.01), Group C (11.8 ± 1.5 to 10.6 ± 1.2 pg/ml, p < 0.01), and Group D (11.5 ± 0.8 to 9.9 ± 0.8 pg/ml, p < 0.01). No significant changes in blood pressure were noted in any of the study groups.

Conclusions: These findings suggest that administration of irbesartan and/or lipoic acid to patients with the metabolic syndrome improves endothelial function and reduces pro-inflammatory markers, factors which are implicated in the pathogenesis of atherosclerosis.

Coronary Artery Disease Extent and Severity is Associated With Pulse Wave Velocity, but Not Central Aortic Augmentation Index

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Background: Although it is proposed that central aortic pressure wave characteristics, particularly augmentation index, influence cardiovascular disease progression and may predict cardiovascular risk, nothing is known of the relationship between central waveform characteristics and the severity and extent of coronary artery disease. We tested the hypothesis that coronary artery disease extent and severity are associated with central aortic waveform characteristics in 40 patients (24 male).

Methods: Central aortic waveforms (2F Millar pressure transducer-lipped catheters) were acquired at the time of coronary angiography for suspected native coronary artery disease. The severity and extent of disease were assessed using 2 previously described scoring systems (Modified Sullivan’s severity score and extent scores). Relationships between disease scores, aortic-radial pulse wave velocity (PWV) and subject demographic features and cardiovascular risk factors were assessed by regression techniques.

Results: Both extent and severity scores were associated with increasing age and male gender (\( P < 0.001 \)) but no other risk factors. Both scores were independently associated with PWV (\( P < 0.001 \)), which entered a multiple regression model prior to age and gender. This association was not related to mean, diastolic or systolic blood pressure. Neither score was associated with any central aortic waveform parameter, including augmentation index, by either simple linear regression or multiple linear regression technique including heart rate and subject demographic features and cardiovascular risk factors.

Conclusion: Aorto-radial PWV, but not central aortic augmentation index, is associated with both the extent and severity of coronary artery disease.

Tetrahydrobiopterin Corrects Escherichia Coli Endotoxin-Induced Endothelial Dysfunction

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Background: Acute inflammation causes endothelial dysfunction, which is partly mediated by oxidant stress and inactivation of nitric oxide (NO). The contribution of depletion of tetrahydrobiopterin (BH4), the cofactor required for NO generation, is unclear. Methods: In this randomized, double-blind, three-way cross-over study, forearm blood flow (FD) responses to acetylcholine (Ach) or glycylarginine (AArg) were assessed before and after 4 hours of administration of Escherichia coli endotoxin (LPS, 20 μg/kg i.v.) in 8 healthy males. The effect of intra-arterial BH4 (500 μg/min), placebo, or vitamin C (24 mg/min) was studied 4 hours after LPS, respectively. Results: Ach-induced forearm vasodilation. LPS decreased FB responses to Ach by 23 ± 6 % (p < 0.05), which was restored to baseline responses by BH4 and vitamin C. BHF responses to GTN were not affected by BH4 or vitamin C. LPS increased leucocyte count, high sensitivity C-reactive protein, heart rate and body temperature and decreased platelet count and vitamin C concentrations. Vitamin C increased forearm plasma concentrations of BH4 from 17.3 ± 3.1 to 23.6 ± 4.2 nmol/l after LPS (p < 0.02). Conclusions: Impaired endothelial function during acute inflammation can be restored by BH4 or vitamin C. Vitamin C may exert some of its effects by increasing BH4 concentrations.

Endothelial-Dependent Vasodilation Does Not Improve With the Atkins’ Diet in Diabetic Subjects

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Background: Vascular endothelial dysfunction has been associated with high-fat diets. We tested the hypothesis that the Atkins’ diet will not improve endothelial function despite potential improvement in metabolic parameters.

Methods: Eight obese (BMI > 30) diabetic subjects were admitted to our Clinical Research Center for 21 days. Subjects received their usual diet for 7 days, then received 14 days of the high-fat/low-carbohydrate induction phase of the Atkins’ diet. Flow-mediated dilation was assessed at baseline, before and after 2 weeks of the Atkins’ diet using brachial arterial ultrasound to measure arterial diameter and blood velocity at baseline, during post-cuff occlusion reactive hyperemia (endothelium-dependent vasodilation (EDV)), and after 0.4 mg of sublingual nitroglycerin (endothelium-independent vasodilation (EVI)). Results: The 2-week Atkins’ diet resulted in an average weight loss of 6.3 ± 2.4 lbs. There was no significant change in total cholesterol, LDL or HDL cholesterol. Triglycerides decreased 25%, from 150 ± 21 to 113 ± 23 mg/dl (p = 0.007). Fasting glucose fell 23%, from 140 ± 9 to 108 ± 5 mg/dl (p = 0.004). Despite these favorable metabolic changes EDV remained unaltered.